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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/583,738	05/31/2000	Hossein A. Ghanbari	018792/0180	2794

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EXAMINER
PORTNER, VIRGINIA ALLEN

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 06/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/583,738	Ghanbari
Examiner	**Art Unit**
Portner	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 4, 2003* .

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *23-33, 35-47, and 49-58* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☒ Claim(s) *51-58* is/are allowed.

6) ☒ Claim(s) *23-33, 35-47, 49, and 50* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 23-33, 35-37, 49-50 and new claims 51-58 are pending.

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 4, 2003, has been entered.

Allowable Subject Matter

2. Claims 51-58 define over the prior art of record and therefore are allowed.

Rejections Maintained

33,35-39, 47,49,50

3. Claims 23-25, 29-30,~~33-39~~,43-44,~~47-50~~ rejected under 35 U.S.C. 102(e) as being anticipated by Merril et al (US Pat 5,688,501; effective filing date of April 5, 1994) .

4. Claims 23-24, 33-~~39~~, 37-38, 47-~~50~~ rejected under 35 U.S.C. 102(b) as being anticipated by Norris (US Pat. 4,957,686).

5. Claims 26 and 40 rejected under 35 U.S.C. 103(a) as being unpatentable over Merrill et al (US Pat 5,688,501; effective filing date of April 5, 1994), in view of Denney (US Pat. 3,793,151).

6. Claims 27 and 41 rejected under 35 U.S.C. 103(a) as being unpatentable over Merrill et al (US Pat 5,688,501; effective filing date of April 5, 1994) in view of He et al (1992).

7. Claims 28 and 42 rejected under 35 U.S.C. 103(a) as being unpatentable over Merrill et al (US Pat 5,688,501; effective filing date of April 5, 1994), in view of Sekaninova et al (1995).

8. Claims 31 and 45 rejected under 35 U.S.C. 103(a) as being unpatentable over Merrill et al (US Pat 5,688,501; effective filing date of April 5, 1994), in view of Bar-Shalom et al (US Pat. 5,213,808).

9. Claim 45 rejected under 35 U.S.C. 103(a) as being unpatentable over Merrill et al (US Pat 5,688,501; effective filing date of April 5, 1994), in view of Tomalia et al (US Pat. 5,714,166).

Response To Arguments

10. The rejection of claims 23-25, 29-30, 33,35-39 47,49,50 ~~[illegible]~~,43-44, ~~[illegible]~~ under 35 U.S.C. 102(e) as being anticipated by Merril et al (US Pat 5,688,501; effective filing date of April 5, 1994) is traversed on the grounds that "Merrill itself does not teach a bacteriophage preparation having a wide host range".

11. It is the position of the examiner Applicant's definition of the phrase "wide host range" includes the meaning": "[T]he expression "wide host range" denotes a bacteriophage that is capable of killing bacteria from a variety of different hosts." Clearly the lambda phage of Merril et al are able to kill bacteria from a variety of different hosts; the reference also claims the utilization of bacteriophages that are genus specific, and thus would infect and kill a plurality of strains and species of each genus of bacteria (see col. 3, lines 45-49; col. 4, lines 45-49 (plurality of pathogens treated); col. 12, lines 4-6; Merril et al, claims 1, 9, 12-13, 15-16).

12. Merrill et al is asserted not to disclose a bacteriophage preparation having a wide host range.

13. It is the position of the examiner that the bacteriophages of Merrill et al are specific for a genus of bacteria which would include a plurality of species and strains (see claim 13, Merrill et al, col. 16, lines 34-39). In example 6, Merrill et al utilized lambda coliphages (see col. 14, line 48-49) which would specifically interact with multiple strains of Escherichia coli based upon the lambda receptor being present in E.coli.

14. Merrill et al is asserted to not teach a composition comprising two or more bacteriophage strains.

15. It is the position of the examiner that each strain of bacteriophage is not required to infect a different bacteria, but the strains must differ one from the other to be considered a separate strain of bacteriophage. The bacteriophage preparations are selected based upon serial passage of the bacteriophages through a host, thus producing a preparation of bacteriophages that represent at least two strains of spontaneous mutants that evidence delayed inactivation by the host defense system (see col. 5, lines 32-47). The isolated mutants (at least two strains) are grown to high titer and administered to an animal in need of treatment (see col. 5, lines 42-46). Merrill et al, through administering a full array of bacteriophages (see col. 7, line 1, Merril et al), accomplishes like that of Applicant's claims, the administration of a single bacteriophage preparation containing a plurality of strains of bacteriophage that enables treatment.

It is also the position of the examiner that more than one process can be used to obtain the administered bacteriophage preparation with the recited functional limitations, one such process is disclosed by Merril et al.

16. Merril et al is traversed on the grounds that the preparation of Merril et al is not purified and non-toxic phage preparation.

17. It is the position of the examiner that the bacteriophage preparation of Merril et al is isolated and purified (see Merril et al, coll. 16, line 27, claim 12) and non-toxic (see col. 15, lines 21-25, the bacteriophage preparation prevented death, thus was non-toxic and effective to kill infecting bacteria) phage preparation. It was noted by the examiner that none of the claims recite any specific levels of toxin present in the preparation. Applicant's arguments are not commensurate in

scope with the instantly claimed invention. The rejection of the claims is maintained for reasons of record.

18. The rejection of claims 23-24, 33-[redacted], 37-38, 47-[redacted] under 35 U.S.C. 102(b) as being anticipated by Norris (US Pat. 4,957,686) is asserted to not teach or disclose a "wide host range" preparation of bacteriophage.

19. It is the position of the examiner that the bacteriophage preparation of Norris comprises two or more strains of bacteriophage (mixtures) which are virulent (parasitic to bacteria) and selected against S.sanguis (Norris, claim 3), and virulent against bacteria normally present in the mouth (see Norris claim 3), specifically defined to include bacteriophages specific for S.aureus(Norris, col. 3, line 19), S.mutans and strains of lactobacillus (see col. 1, line 25 and col. 3, line 2).

The bacteriophage that would infect one strain of S.sanguis, would also infection another strain of S.sanguis with the same or equivalent receptor. In light of the definition of "wide host range" encompassing the embodiment of infecting two different strains of the same bacteria, the bacteriophage of Norris would function in the same or equivalent manner as now recited in the claims. While the bacteriophage of Norris are species specific (see col. 3, lines 28-30), the bacteriophage would infect a plurality of strains of a single species. The composition of Norris also contains two or more bacteriophages for parasitic bacteria of the mouth. Applicant's arguments are not commensurate in scope with the instantly claimed invention.

20. The rejection of claims 26 and 40 under 35 U.S.C. 103(a) as being unpatentable over Merrill et al in view of Denney (US Pat. 3,793,151) is traversed on the grounds that the "examiner has

mistakenly equated Merril et al's disclosure regarding an LD50 dose of bacteria to mice with the concept of wide-host range phage in Applicant's invention.

21. It is the position of the examiner that contrary to Applicant's assertion, the examiner has not mistakenly equated Merril et al's disclosure regarding an LD50 dose of bacteria to mice with the concept of wide-host range phage in Applicant's invention. Wide host range involves killing but does not require any specific percentage killing. The functional limitation with respect to an in vitro assay for bacteriophage killing, defines the ability of the bacteriophage to infect and to function as a lethal entity.

It is the position of the examiner that the claimed method recites a single methods step of "administering" a composition and does not require an in-vitro assay to be carried out, but the preparation must have the capability to function in an in vitro assay to kill 50% of the bacteria in that assay. Bacteriophage that are capable to providing protection in vivo through killing an LD_{50} dosage of bacteria (the bacteriophages of Merrill et al, Example 6, col. 14 to col. 15; and col. 11, lines 64-67) , would also have the capability of functioning to kill 50% of the same bacteria in an **in-vitro assay**. Both assay measure killing and define the administered composition as one that is effective to provide protection through killing at least 50% of the bacteria, to include bacterial elimination (100% bacterial cell death).

22. It is asserted that and LD50 dose refers to bacteria and not to bacteriophage characteristics.

23. While the examiner agrees that LD50 defines a dose of bacteria able to kill 50% of the experimental subjects, it is also the position of the examiner that the bacteriophage preparation of Merril et al was functionally defined to be effective to prevent death of animals that had and LD50 dose of bacteria administered thereto. A bacteriophage that is defined to be functionally effective

to kill a lethal dose of bacteria for 50% of the subjects, would evidence the functional capability to kill 50% of the bacteria in an in vitro assay as well.

24. Denny is asserted to not remedy the deficiencies of Merrill et al, specifically a wide host range bacteriophage for Streptococcus pyogenes.

25. It is the position of the examiner that Denny was cited to show a S.pyogenes specific phage (see Denny: col. 2, lines 56-66) that is able to infect any unencapsulated strain of S.pyogenes. Bacteriophage preparations specific for two or more strains of S.pyogenes that are unencapsulated would define a wide host range bacteriophage by Applicant's definition. The rejection is maintained for reasons of record.

26. The rejection of Claims 27 and 41 under 35 U.S.C. 103(a) as being unpatentable over Merrill et al in view of He et al (1992) is traversed on the grounds the He et al does not disclose a wide host range bacteriophage as defined by Applicant.

27. It is the position of the examiner that the instant specification defines a plurality of embodiments that define the meaning of the phrase "wide host range". As the claims broadly recite any of the provided definitions, and the fact that He et al does disclose wide host range bacteriophages (see page 591, Results section, phage O-I, lysed Salmonella subgenus strains I, II, IIIa and IIIb, last paragraph to greater than 50%; see page 592, col. 1, paragraph (vi), where phage "Sh" lysed both Shigella and Ecoli to greater than 50%; C.freundii phage ϕI lysed 50.% of Citrobacter cultures, specifically 3, 222 strains). Clearly He et al discloses a plurality of wide host range bacteriophages, to include bacteriophages for C.freundii (see Table 3, page 592).

28. The rejection of claims 28 and 42 under 35 U.S.C. 103(a) as being unpatentable over Merrill et al in view of Sekaninova et al (1995) is traversed on the grounds that Sekaninova et al is asserted not to remedy the deficiencies of Merrill et al and Sekaninova does not disclose a bacteriophage with a "wide host range".

29. It is the position of the examiner that the Merrill et al reference is not deficient as asserted (see discussion above), and Sekaninova et al showed 5 bacteriophages that were specific for Klebsiella oxytoca, as well as Klebsiella pneumoniae through teaching that the "biotypes of Klebsiella, i.e. K.pneumoniae and K.oxytoca, were identically sensitive to some of the phages 1, 2, 3, 8 and 106, particularly to phages 2 and 3". Thus the bacteriophages are disclosed to be "wide host range" bacteriophages for Klebsiella, to include specific for Klebsiella oxytoca (see abstract, last three lines). The bacteriophages are apart of the Polish Collection of Microorganism of the Polish Academy of Sciences, Wroclaw (see page 81, col. 1, paragraph 5, second sentence).

30. The rejection of claims 31 and 45 under 35 U.S.C. 103(a) as being unpatentable over Merrill et al in view of Bar-Shalom et al (US Pat. 5,213,808) is traversed on the grounds that the controlled release article of Bar-Shalom et al is not a liposome.

31. While the controlled release article of Bar-Shalom et al is not a liposome, the controlled release article of Bar-Shalom et al is taught to comprise liposomes that contain an active agent, the active agent being defined to include bacteriophages. Bar-Shalom et al (abstract, col. 9, lines 41-57; col. 9, lines 65-67 and col. 10, lines 1-3) shows liposomes for the purpose of delivering an active agent to a mammal, wherein an active agent is a bacteriophage. The patent specifically teaches "the composition is in addition suitable for the delivery of"(col. 9, lines 41-42)

"bacteriophages, e.g. as vaccines" (see col. 9, line 52). Bar-Shalom et al teaches the combination of vaccine bacteriophages incorporated in liposomes in the controlled delivery article.

32. The rejection of claims 45 under 35 U.S.C. 103(a) as being unpatentable over Merrill et al in view of Tomalia et al (US Pat. 5,714,166) is traversed on the grounds that a liposome and a dentrimer are not the same.

33. It is the position of the examiner that the Merrill et al reference is not deficient as asserted (see discussion above), and the dentrimers of Tomalia et al are not liposomes. The rejection of claim 31 has been removed. The combination of the two references teach the utilization of dentrimers as a carrier means for the delivery of high concentrations of a phage material (col. 1, lines 39-43; col. 47, lines 1-3) and the dentrimer of Tomalia provides a means for the controlled and targeted delivery of bacteriophage in a high concentration to a host. The rejection is maintained for reasons of record.

34. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp
June 11, 2003

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